May 2010

Office of Education, Division of Intramural Research
National Heart, Lung, and Blood Institute

FELLOWS NEWSLETTER

The Fellows Newsletter is published monthly by the Office of Education, Division of Intramural Research, National Heart, Lung, and Blood Institute and distributed to NHLBI DIR members to promote the interest of DIR Fellows.

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From the Director of the Office of Education

We thank all who participated in organizing the successful retreat in Baltimore, especially Angela Theofilos and Aurora Taylor, and the members of the Fellows Advisory Committee. We also thank our poster presenters and speakers for an outstanding job. Now that the 2010 retreat is finished, we are beginning to plan the next one. So if you'd like to participate, we welcome new members to the Fellows Advisory Committee. Committee members also get to assist the Office of Education in formulating policies that assist all Fellows in their Career Development.

We will soon be joined by a large number of summer students. Mentoring a summer student can be a rewarding experience, and also allows you to add this skill to your C.V. So if your lab has a summer research, take an interest in their work.

Finally, the Office of Education is trying to increase the number of rotation opportunities for Fellows. When we approach many of these organizations, their first response is "send me some C.V.'s and we can place them". So towards that end, if you are interested in exploring a rotation opportunity with any of our current organizations, or would like to be placed in the near future, send your current C.V. to the Office of Education and we'll be ready to recommend you.

"Don't Be Such a Scientist"

by Randy Olson
Reviewed by Dr. Herbert Geller,
Director, Office of Education

When was the last time you sat through a boring scientific lecture? Chances are, it was not too long ago. If you want to avoid this problem with your own talks, then Randy Olson's book "Don't Be *Such* A Scientist" is a must-read. Olson, a Ph.D. in Marine Biology, walked away from a tenured faculty position to go to film school in Hollywood. He describes his film school experiences in excruciating detail, with the main theme that good communication cannot simply be based on (cont'd on p.2)

The Fellows Seminar Series presents:

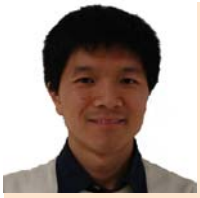
Chromatin Insulators and Nuclear Organization

Victor Corces, Ph.D.
Professor of Gene and Cell Medicine,Emory University

Tuesday,May11th, 2010
11:00am to 12:00pm
Building 50, room 1328/1334

New NHLBI Fellows

Qiuting Ren, Ph. D., is Visiting Fellow in the Genetics and Developmental Biology Center under the mentorship of Dr. Hong Xu. Dr. Ren received her Ph. D. in Biochemistry and Neurobiology from Johns Hopkins University School of Medicine in Baltimore, Maryland. She was a member of the Technology and Life Science Entrepreneurs Boot Camp at Johns Hopkins. Dr. Ren's initial research project involves Mitochondria genetics in Drosophila.



Peng Tao, Ph.D., is a Research Fellow in the Laboratory of Computational Biology under the mentorship of Dr. Bernard Brooks. Dr. Tao earned his Ph.D. in Physical Chemistry from Ohio State University in Columbus, Ohio. Dr. Tao received a Special Honorable Mention at the Albert L. Henne Research Forum at Ohio State. His initial research project is using combined quantum mechanical and molecular mechanical method to investigate reaction mechanism of enzymatic system.

transmitting information – it needs to evoke an emotional response in the listener. His major observation may seem rather off-putting to those of us who deal with data: we are supposed to be dispassionate and neutral. Either a hypothesis is true or it is false, and we are supposed to be happy whatever way it comes out. However, that's not the way the human mind works. The centers of emotion are not in our cerebral cortex, but rather in the limbic system, which reacts to a different set of stimuli. And so we have to make our presentations appeal to both the cortical neurons (the data should be convincing) and the subcortical systems (the data should have some emotional value other than being statistically significant).

The subtitle of the book is "Talking substance in an age of style" and is mainly directed at scientific communication to the public. In this vein, his argument is that, while one should not distort the truth, it is often necessary to simplify and distill the essence of the observation to a simple, easily understood point. One can easily see that this applies to all of our scientific communications as well. (I cannot tell you how many presentations I've seen that had *too* much data, rather than not enough). There are five major chapters, including those titled "Don't be so cerebral", "Don't be so literal minded", "Don't be such a poor storyteller", and "Don't be so unlikable". Each one is a mixture of his own observations leading to cogent advice for the scientist-communicator. While some of his anecdotes can be somewhat superficial, the overall message is one that each of needs to absorb.

Randy Olson also maintains a web site and a blog entitled "The Benshi" (http://thebenshi.com/) which continues the discussion where the book ends. I found the blog just as entertaining as the book, and it provides a continual reminder of how far we need to go to improve our communication skills.

Congratulations to the 2010 NHLBI DIR Scientific Retreat Poster Winners!

Edmund Chen,
PostBac

Dr. Cynthia St. Hilaire,
PostDoc

Dr. Michael Lerner,
PostDoc

Dr. Xianglan Yao,
Staff Scientist

Recent Publications by NHLBI Fellows

Bektas, M., Allende, M. L., Lee, B. G., Chen, W. P., **Amar, M. J.**, Remaley, A. T., Saba, J. D., & Proia, R. L. (2010). Sphingosine 1-Phosphate Lyase Deficiency Disrupts Lipid Homeostasis in Liver. Journal of Biological Chemistry 285, 10880-10889.

Chen, K., Delaglio, F., & Tjandra, N. (2010). A practical implementation of cross-spectrum in protein backbone resonance assignment. Journal of Magnetic Resonance 203, 208-212.

Dagur, P. K., Tatlici, G., Gourley, M., Samsel, L., Raghavachari, N., Liu, P. C., Liu, D. L., & Mccoy, J. P. (2010). CD146+T Lymphocytes Are Increased in Both the Peripheral Circulation and in the Synovial Effusions of Patients with Various Musculoskeletal Diseases and Display Pro-inflammatory Gene Profiles. Cytometry Part B-Clinical Cytometry 78B, 88-95.

Dmitrieva, N. I., Chen, H. T., Nussenzweig, A., & Burg, M. B. (2009). Knockout of Ku86 accelerates cellular senescence induced by high NaCl. Aging-Us 1, 245-253.

Fernandez-Llama, P., Khositseth, **S., Gonzales, P. A.**, Star, R. A., Pisitkun, T., & Knepper, M. A. (2010). Tamm-Horsfall protein and urinary exosome isolation. Kidney International 77, 736-742.

George, A. K., Derbyshire, J. A., **Saybasili, H., Saikus, C. E.**, Kocaturk, O., Guttman, M. A., McVeigh, E. R., Lederman, R. J., & Faranesh, A. Z. (2010). Visualization of Active Devices and Automatic Slice Repositioning ("Snap To") for MRI-Guided Interventions. Magnetic Resonance in Medicine 63, 1070-1079.

Kang, H., Jung, J. W., Kim, M. K., & Chung, J. H. (2009). CK2 Is the Regulator of SIRT1 Substrate-Binding Affinity, Deacetylase Activity and Cellular Response to DNA-Damage. Plos One 4.

Lin, B. Y., Wang, J., Hong, X., Yan, X. W., Hwang, D., Cho, J. H., Yi, D., Utleg, A. G., Fang, X. F., **Schones, D. E.,** Zhao, K. J., Omenn, G. S., & Hood, L. (2009). Integrated Expression Profiling and ChIP-seq Analyses of the Growth Inhibition Response Program of the Androgen Receptor. Plos One 4.

Liu, X., **Shu, S.**, Hong, M. S. S., Yu, B., & Korn, E. D. (2010). Mutation of Actin Tyr-53 Alters the Conformations of the DNase I-binding Loop and the Nucleotide-binding Cleft. Journal of Biological Chemistry 285, 9729-9739.

Majerciak, V., Kruhlak, M., **Dagur, P. K.**, Mccoy, J. P., & Zheng, Z. M. (2010). Caspase-7 Cleavage of Kaposi Sarcoma-associated Herpesvirus ORF57 Confers a Cellular Function against Viral Lytic Gene Expression. Journal of Biological Chemistry 285, 11297-11307.

Pasapera, A. M., Schneider, I. C., Rericha, E., Schlaepfer, D. D., & Waterman, C. M. (2010). Myosin II activity regulates vinculin recruitment to focal adhesions through FAK-mediated paxillin phosphorylation. Journal of Cell Biology 188, 877-890.

Pfefferkorn, C. M. & Lee, J. C. (2010). Tryptophan Probes at the a-Synuclein and Membrane Interface. Journal of Physical Chemistry B 114, 4615-4622.

Phillips, D., ten Hove, M., Schneider, J. E., Wu, C. O., Sebag-Montefiore, L., **Aponte, A.** M., Lygate, C. A., Wallis, J., Clarke, K., Watkins, H., Balaban, R. S., & Neubauer, S. (2010). Mice over-expressing the myocardial creatine transporter develop progressive heart failure and show decreased glycolytic capacity. Journal of Molecular and Cellular Cardiology 48, 582-590.

Saybasili, H., Faranesh, A. Z., **Saikus, C. E.**, Ozturk, C., Lederman, R. J., & Guttman, M. A. (2010). Interventional MRI Using Multiple 3D Angiography Roadmaps With Real-Time Imaging. Journal of Magnetic Resonance Imaging 31, 1015-1019.

Schroeder, J. L., **Luger-Hamer, M.**, Pursley, R., Pohida, T., Chefd'Hotel, C., Kellman, P., & Balaban, R. S. (2010). Subcellular Motion Compensation for Minimally Invasive Microscopy, In Vivo Evidence for Oxygen Gradients in Resting Muscle. Circulation Research 106, 1129-U271.

Wang, S. N., Zhou, Y. F., **Seavey, C. N., Singh, A. K.,** Xu, X. L., Hunt, T., Hoyt, R. F., & Horvath, K. A. (2010). Rapid and dynamic alterations of gene expression profiles of adult porcine bone marrow-derived stem cell in response to hypoxia. Stem Cell Research 4, 117-128.

Wu, J. J., Quijano, C., Chen, E., Liu, H. J., Cao, L., Fergusson, M. M., Rovira, I. I., Gutkind, S., Daniels, M. P., Komatsu, M., & Finkel, T. (2009). Mitochondrial dysfunction and oxidative stress mediate the physiological impairment induced by the disruption of autophagy. Aging-Us 1, 425-437.

THE SCIENCE BEAT

By Nisha Narayan, Ph.D.

***Pasapera AM**, Schneider IC, Rericha E, Schlaepfer DD, Waterman CM. Myosin II activity regulates vinculin recruitment to focal adhesions through FAK-mediated paxillin phosphorylation. Journal of Cell Biology (2010) 188(6): 877-90*

Molecular motors are tiny biological machines that regulate intracellular movement in living organisms. The force that a cell imparts on its extracellular environment depends largely on the cellular forces developed by motors such as Myosin IIs acting in the actin cytoskeleton. This is in turn associated with the extracellular matrix (ECM) through transmembrane integrins that collect to form mechanical tension sensing organelles called focal adhesions (FAs). The cytoplasmic integrin tails serve as platforms for recruiting FA-associated proteins, which impact FA function in signaling pathways promoting differentiation, cell division and apoptosis, and link the ECM to the cytoskeleton. In an attempt to elucidate tension-mediated FA maturation – the process by which FAs recruit cytoplasmic proteins in response to mechanical strain – the authors looked for the recruited proteins in a contractility-dependent manner and sought an explanation for their myosin II-sensitive FA association.

To define myosin-II mediated FA maturation, they inhibited myosin II in mouse embryonic fibroblasts (MEFs) using chemical inhibitors such as the myosin-II specific blebbistatin, and characterized the consequent effects of restraining contraction. Using immunofluorescent techniques, they found that three different kinds of myosin II inhibition, led to a reduction in adhesion size, distorted cell morphology and increased migration rate of the cells. Next they looked at the effect of actomyosin activity on adhesion by looking at the myosin II dependence of the localization of an adaptor protein named Paxillin – a component of newly formed adhesions. In both control and blebbistatin-treated cells, paxillin was found to colocalise with PhosphoTyrosine (PY)-containing adhesions in spite of the drug's effect on adhesion size and distribution, actin organization and myosin II contractility, making it a good adhesion marker for further experiments. They then examined several essential FA proteins and observed that though the recruitment of paxillin, talin, and β1 integrin to adhesions is independent of myosin II activity, FAK (Focal Adhesion Kinase), zyxin, vinculin and α-actinin required myosin II contraction. They hypothesized subsequently that strong binding affinity to adhesions might take priority over actomyosin dependence in the recruitment of proteins to adhesions. By performing FRAP (Fluorescence Recovery After Photobleaching) analysis, they found varying binding intensities for different proteins to adhesions,

(cont'd on p.5)

2010 NHLBI DIR Scientific Retreat Group Picture

with the adaptor protein vinculin exhibiting particularly stability. They thus chose to focus on this protein and using immunofluorescence techniques, discovered that its myosin II-dependent recruitment was reversible, occurs in a wide range of cell types in the physiologically relevant contexts of adhesion maturation during cell migration. They then established with immunoprecipitation techniques that vinculin interacts with, and is recruited by paxillin to adhesions and that this interaction is dependent on the tyrosine phosphorylation of paxillin on Y31/118 by FAK in a myosin-II dependent manner. This was further ascertained by showing that using a paxillin Y31/118 phosphomimic was adequate to promote the paxillin-vinculin interaction and to recruit vinculin to adhesions. They however could not establish the essentiality of FAK in these events because of the difficulty in assessing its singular effects in this context. Hence, there are additional FAK-independent pathways that recruit vinculin to stable adhesions.

This study elucidates a clear mechanism for the myosin II-mediated vinculin adhesion recruitment and its role in adhesion maturation. Though it is obvious that there are other trails yet to be discovered in the field of adhesion biology, these set of observations give us an improved understanding of the internal work forces of the cell.

Congratulations to the 2010 NHLBI DIR Scientific Retreat Outstanding Mentor Award Winners, Dr. Michael Sack and Dr. Trairak Pisitkun!

New Rotation Opportunities for Postdoctoral Fellows

NHLBI has established a mechanism by which Postdoctoral Fellows can participate in rotations to explore career opportunities. Fellows who are interested in doing a rotation in the following areas this year should contact the Office of Education for more information:

- FASEB (Federation of American Societies for Experimental Biology) - Science Policy
www.faseb.org
- Adjuvant Global Advisors, Bethesda - Science Business Development and Advocacy
www.adjuvant.com
- The World Bank - International Science Policy
www.worldbank.org

2010 NHLBI DIR Retreat Pictures